Eur J Vasc Endovasc Surg 10, 156–161 (1995)

Carbon Dioxide: An Alternative to Iodinated Contrast Media*

S. W. Yusuf[1], S. C. Whitaker[1], D. Hinwood[1], M. J. Henderson[2], R. H. S. Gregson[1], P. W. Wenham[1], B. R. Hopkinson[1] and G. S. Makin[1]

[1]Vascular Unit, University Hospital, Nottingham and [2]Department of Radiology, Birmingham Heartlands Hospital, U.K.

Objectives: *To study the use of carbon dioxide as a contrast medium for arteriography.*
Methods: *Carbon dioxide was used as a contrast medium for intra-arterial digital subtraction lower limb angiography in 12 examinations on 11 patients.*
Results: *No complication was encountered and no significant changes occurred in the arterial pH, $PaCO_2$ and PaO_2. The quality of images as assessed by an independent observer was adequate for the majority of the vessels (77%).*
Conclusions: *Carbon dioxide is a safe alternative in patients at an increased risk of adverse reaction to iodinated ionic or non-ionic contrast medium and is very cheap.*

Introduction

Modern non-ionic low osmolar contrast media are relatively safe and produce good quality angiographic images. However, their use is not entirely free from problems in certain situations. Nephrotoxicity is a well recognized side effect of intravascular contrast. The risk of renal damage is particularly high in patients with diabetes, hypertension, dehydration, multiple myeloma and in the presence of impaired renal function;[1] conditions which often co-exist with peripheral vascular disease. The risk of allergic reaction to iodine containing contrast has been estimated to be 4–7% in atopic individuals,[2] rising to 38% in those with a previous history of adverse reaction to contrast.[3] Rapid injection of contrast can result in pulmonary oedema particularly in patients with poor ventricular function.[4] Carbon dioxide has been used successfully in the past as a negative contrast for cystogram,[5] arthrogram[6] and angiogram.[7,8] In the present study CO_2 has been evaluated in a prospective controlled study as an angiographic contrast medium during digital subtraction peripheral angiography.

Patients and Methods

Twelve examinations were performed on 11 patients with a median age of 72 years (range 67–82 years). All the patients were being investigated for peripheral vascular disease. Approval was obtained from the University Hospital Ethics Committee and informed consent was obtained from the patients. Angiography was performed with both Iopamidol (Niopam, E. Merck Ltd) and Carbon dioxide in 9/12 procedures and CO_2 was used alone in three examinations. Of these three procedures two were performed in a patient with a history of severe adverse reaction to iodinated contrast and another patient had refractory cardiac failure. Anterior femoral wall puncture technique was used for the introduction of a 5 F angiographic flush catheter. Iopamidol injections were carried out with the catheter in the abdominal aorta. For CO_2 injections the catheter was withdrawn into the external iliac and direct intra-aortic injection was avoided. Medical grade CO_2 (BOC Medical gases, Guildford, Surrey U.K.) was drawn into a 60 ml syringe from a laparoscopic insufflator. The syringe was flushed with CO_2 a few times to eliminate any air and ipsilateral images were obtained following rapid hand injection of 50 ml of CO_2 for each run. The leg was elevated approximately 20° to facilitate the forward flow of CO_2 aided by buoyancy. Arterial blood gases were obtained before and within 1 min of completion of the study in 10/12 cases and analysed for pH, $PaCO_2$ and PaO_2 on a blood gas analyser.

*Presented at the 8th annual meeting of the European Society for Vascular Surgery, Berlin, Germany (September 1994).

Please address all correspondence to: S.W. Yusuf, Vascular Research Fellow, E Floor West Block, University Hospital, Nottingham NG7 2UH, U.K.

1078–5884/95/060156 + 06 $12·00/0

Paired images obtained with Niopam and CO_2 were blindly assessed by MJH (a vascular radiologist from another region) without any knowledge of the nature of the study. He was asked to select the better image in each pair and using it as the standard, grade individual vessels in the other image as adequate or inadequate on the criteria that no important clinical information was missing or misinformation was present. Statistical analysis was performed by using Wilcoxon paired rank signed test for comparing the changes in arterial blood before and after the procedure.

Results

(1) No complication occurred in any of the procedure.
(2) The median volume of CO_2 used was 200 ml (range 200–300 ml).
(3) There was no significant change in the arterial pH, $PaCO_2$ and PaO_2 following CO_2 angiography (Figs. 1, 2 and 3).
(4) In each pair the image obtained with Niopam was selected as the better image.
(5) The quality of images were totally adequate in the Femoral and popliteal regions. Overall 23% of the

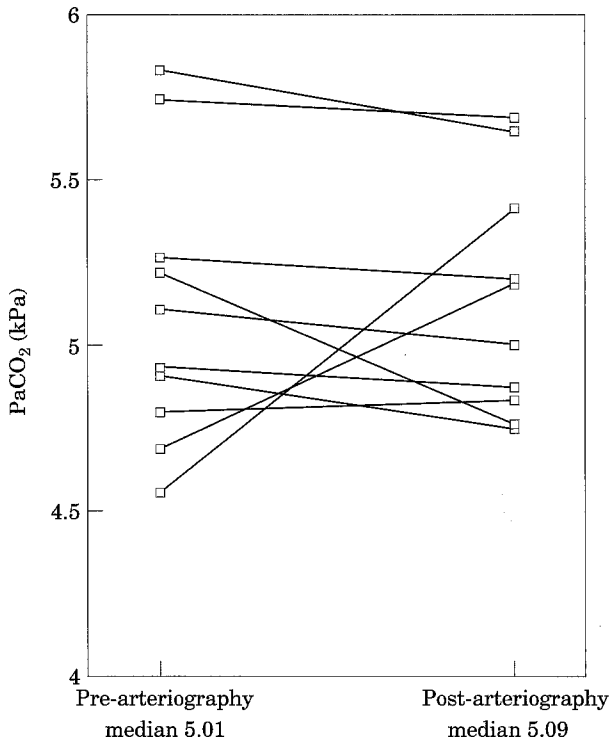

Fig. 2. Changes in $PaCO_2$ following CO_2 angiography.

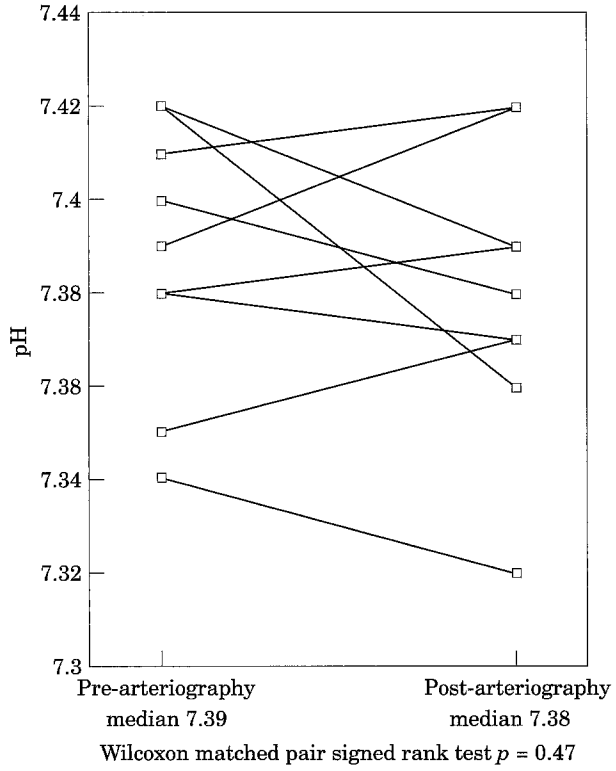

Fig. 1. Changes in the arterial pH following CO_2 angiography.

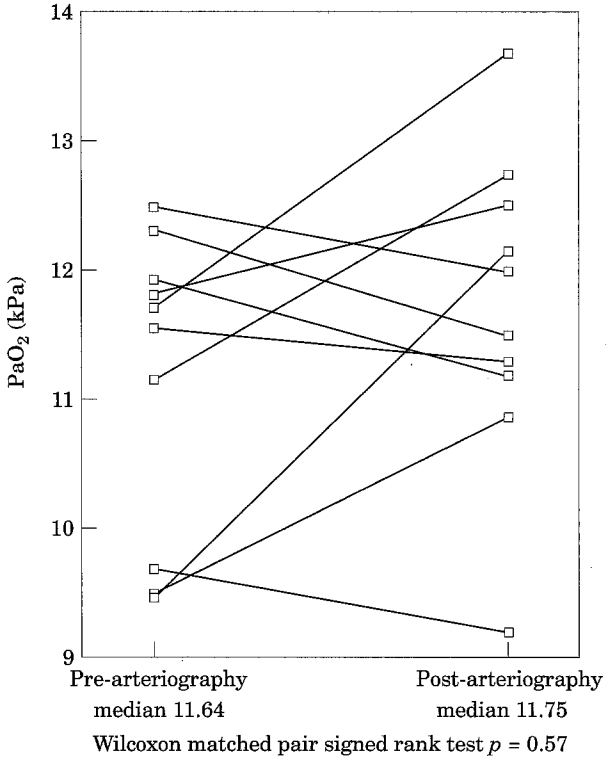

Fig. 3. Changes in PaO_2 following CO_2 angiography.

images were deemed to be inadequate. Of these 6% were iliac and 17% were tibial images.

(6) Bilateral superficial femoral angioplasties were performed on two separate occasions on one patient who had a history of major adverse reaction to iodinated contrast with good radiological, haemodynamic and clinical result (Fig. 4).

(7) One diagnostic examination was successfully carried out with a 20 G cannula placed in the femoral artery.

Discussion

Carbon dioxide (CO_2) has been used as a radiological contrast medium for more than three decades.[5] As an angiographic contrast medium CO_2 has been in use since 1968 by Bendib *et al.*[7] who has reported uncomplicated use of intravenous CO_2 in more than 1600 patients for diagnostic study of the right side of the heart. In patients with peripheral vascular disease CO_2 was first used intra-arterially as a vasodilator agent by Bartley *et al.*[9] more than 20 years ago. During subsequent study on therapeutic use of CO_2 in patients with peripheral occlusive arterial disease by the same group,[10] it was observed that CO_2 delineated the artery by acting as a negative radiological contrast. Since then Hawkins and Herrera[8] have reported safe use of CO_2 for angiography in more than 300 patients. However, in Europe the use of CO_2 as a contrast medium for peripheral angiography has not been widely reported. Moreover, the quality of images obtained during peripheral digital subtraction arteriography using CO_2 and non-ionic iodinated contrast has not been compared in the past.

The important risk factors related to contrast

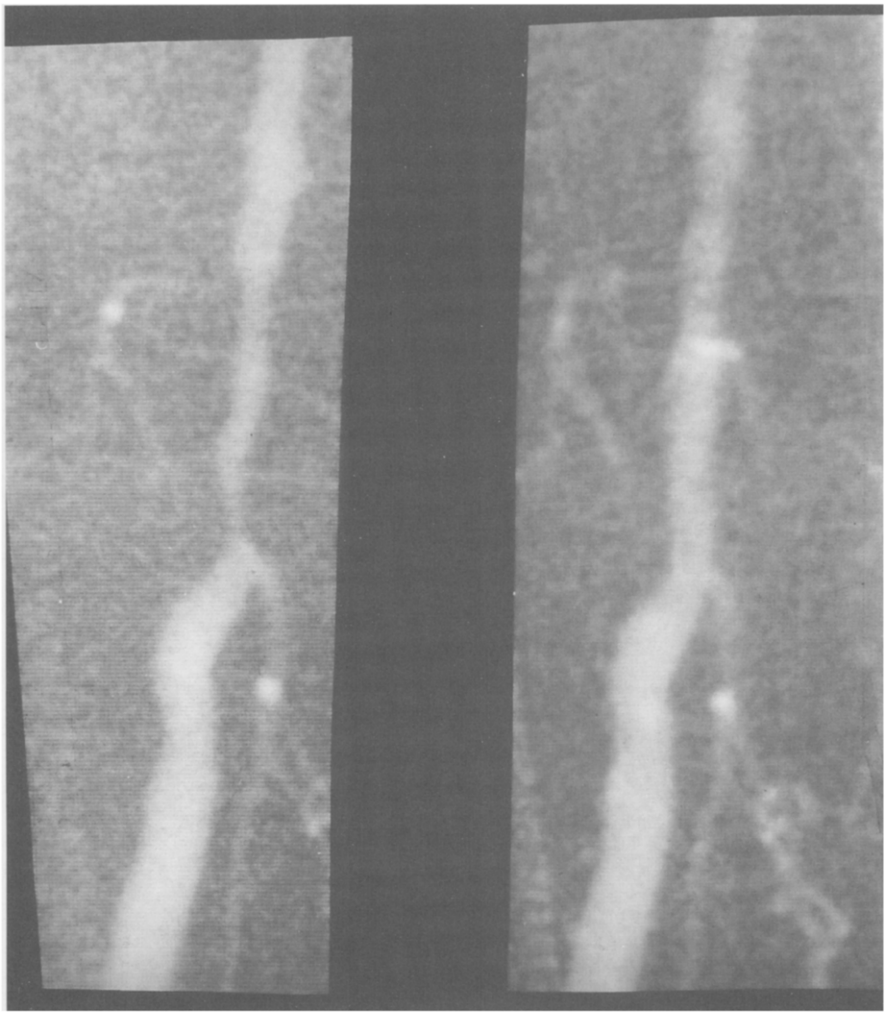

Fig. 4. (left) Superficial femoral artery stenosis demonstrated with CO_2 angiography. (right) Post angioplasty.

medium induced renal damage are pre-existing renal insufficiency, diabetes mellitus with the risk becoming more significant in patients with diabetic nephropathy. In a prospective study of non diabetic patients with impaired renal function undergoing intravenous urography (IVU) the incidence of acute renal failure has been reported to be as high as 62%.[12] Patients undergoing IVU are more likely to have impaired renal function than those undergoing arteriography but the volume of contrast used for peripheral angiography is nearly three to four times greater than the volume used for IVU and there is some suggestion that the nephrotoxicity may be dose related. CO_2 could therefore be used as an alternative for arteriography in patients with impaired renal function, diabetic nephropathy and multiple myeloma who are at an increased risk of contrast induced renal damage.

The iodine load following injection of 100 ml of triiodinated non ionic contrast medium could be 3–4 g. This could produce hyperthyroidism in euthyroid

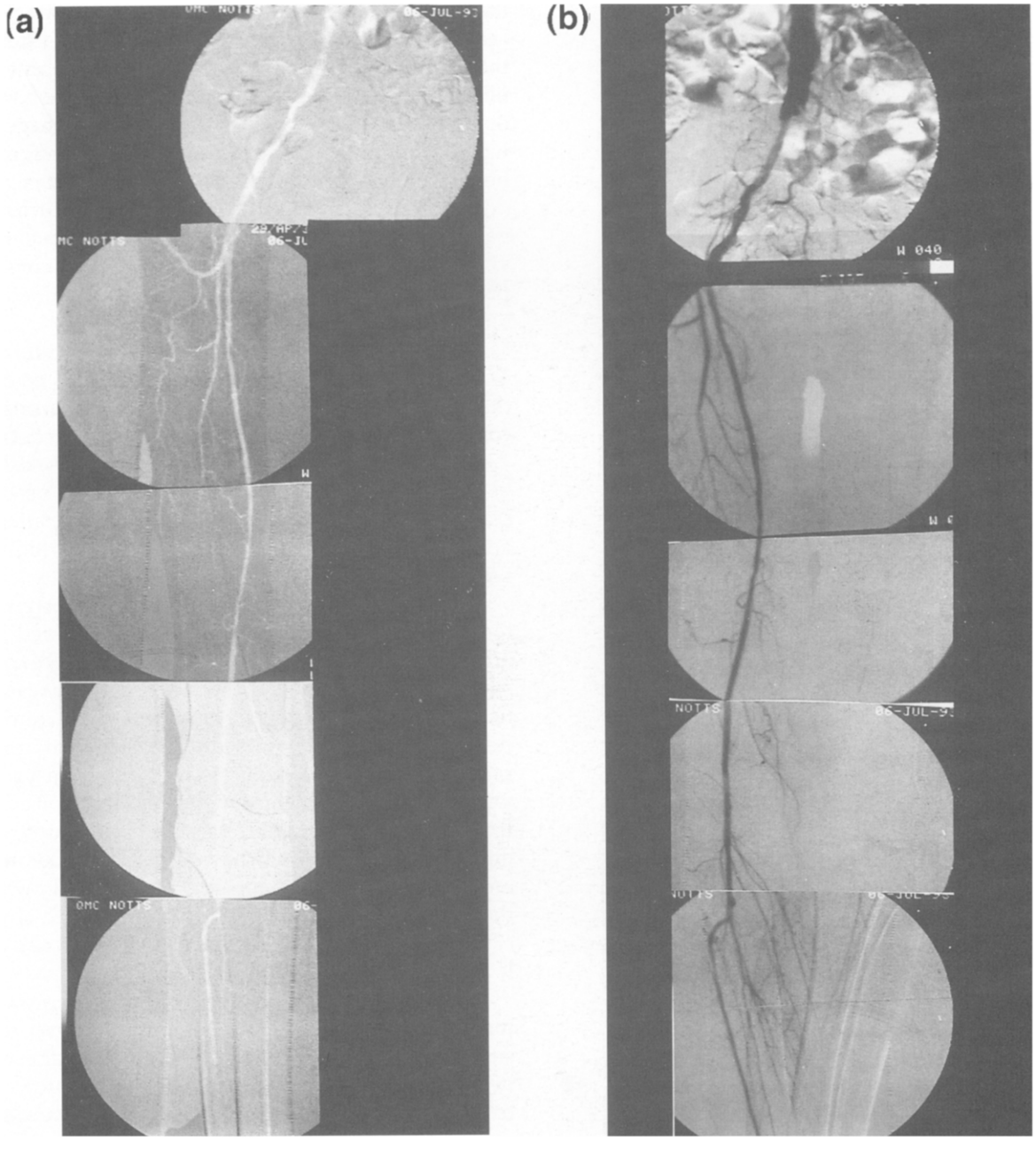

Fig. 5. (a) Ipsilateral digital subtraction angiography with intra-arterial CO_2 injection. (b) Paired image obtained with Niopam 300 (Merck Ltd.).

individuals with autonomous thyroid nodules[13] and CO_2 again offers a safe alternative in such patients.

In patients with impaired ventricular function, injection of osmolar contrast medium can lead to pulmonary oedema particularly when the volume injected exceeds 200 ml.[4] CO_2 does not add to the circulatory fluid load and could again be useful in such patients.

One other advantage of CO_2 is its low viscosity which is almost 400 times less than the conventional mono acid monomeric salt contrast medium.[10] This means that angiography can be performed via relatively fine catheters and small puncture in the femoral artery. In the present study we were able to perform the procedure with a 20 G cannula (Viggo, Spectramed) instead of the standard 4 or 5 F catheter.

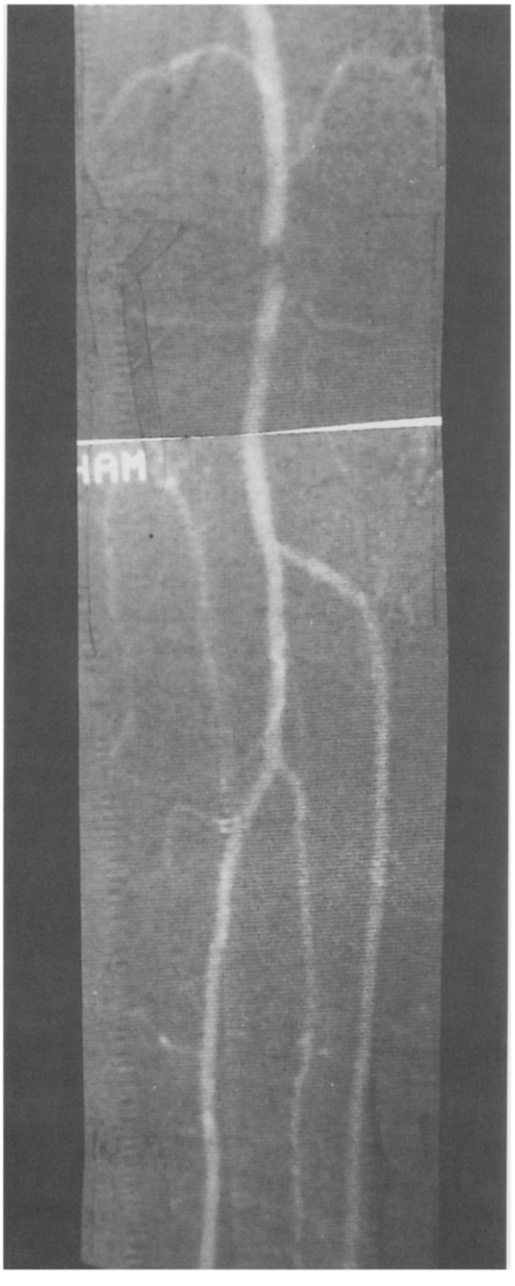

Fig. 6. Popliteal and tibial arteries demonstrated with CO_2 intra-arterial digital subtraction angiography.

Because there is some evidence from animal studies that CO_2 may be neurotoxic,[14] we avoided direct aortic injection to avoid any adverse effect on the spinal cord. The visualisation of the proximal iliac was therefore dependent upon reflux of the CO_2 and could account for the 6% of the inadequate images being in the iliac region (Fig. 5a). It seems likely that antegrade filling of the iliac artery from aortic injection would overcome this problem. Of the inadequate images 17% were in the tibial region. In some studies fragmentation of the column of CO_2 was seen in the tibial vessel (Fig. 5a). It appears to be related to slow transit in patients with poor ventricular function. However, the visualisation of tibial vessels was not a consistent problem and good images were also obtained (Fig. 6).

Cost is an important consideration. A cylinder of CO_2 containing 450 l of medical grade CO_2 costs less than 100 ml of non-ionic contrast. In other words, the contrast cost of angiography with non-ionic contrast is 1000 fold greater than CO_2. However, the overall cost benefit may not be a significant one if CO_2 is used only selectively in a relatively small number of patients at an increased risk of adverse reaction to iodinated intravascular contrast.

In the present study no complication was encountered and no significant changes were observed in the arterial pH and gases. This is somewhat expected since the volume of CO_2 used for each study was close to the amount excreted by the body each minute at rest. CO_2 injection not only enabled diagnostic angiography but angioplasty was also performed in a patient with bilateral SFA stenosis who had a major adverse reaction to iodinated contrast in the past. Duplex scan guided angioplasty which requires two operators is another technique that can enable angioplasty without the use of intravascular contrast.[15] With further experience it may provide another safe alternative for localised studies and angioplasty.

In summary, CO_2 is safe and effective as a contrast medium during peripheral angiography with digital subtraction imaging. It could be used as an alternative in patients with history of adverse reaction to iodinated contrast and those individuals who are at an increased risk of renal damage and pulmonary oedema from the conventional intravascular contrast.

References

1 Ansell G. Adverse reactions profile: Intravenous iodinated radiocontrast media. *Prescribers' Journal* 1993; **33**: 82–88.
2 Witten DM, Hirsch FD, Hartman GW. Acute reactions to urographic contrast medium. Incidence, clinical characteristics and relationship to history of hypersensitivity state. *Am J Roentgenol* 1973; **119**: 832–840.
3 Ansell G, Tweedie MCK, West CR. The current status of reactions to intravenous contrast media. *Invest Radiol* 1980; **15**: S32–S39.
4 Malins AF. Pulmonary oedema after radiological investigation of peripheral occlusive vascular disease. Adverse reaction to contrast material. *Lancet* 1978; i: 413–415.
5 Bartley O, Helander CG. Double contrast cystography in tumours of urinary bladder. *Acta Radiol* 1960; **54**: 161.
6 Goldberg RP, Hall FM, Wyshak G. Pain in knee arthrography: Comparison of air versus Carbondioxide and reaspiration versus no aspiration. *Am J Roentgenol* 1981; **136**: 377–379.
7 Bendib M, Toumi M, Boudjellab A. Carboxyangiographie et carboxyangiographie èlargie en cardiologie. *Ann Radiol* 1977; **20**: 673–686.
8 Hawkins IF, Herrera MA. Carbon dioxide has promise as arterial contrast agent. *Diagnostic Imaging* 1985; 82–84.
9 Bartley O, Lantz B, Nordqvist P. Insufflation of Carbon dioxide into a lower extremity - an alternative to amputation? *Opusc Med* 1972; **17**: 156–162.
10 Lantz BMT, Nordqvist P, Henning A. Effect of intra-arterial carbon dioxide insufflation on occlusive arterial disease in the lower leg. *Acta Radiologica Diagnosis* 1978; **19**: 1033–1044.
11 Hawkins IF. Carbon dioxide digital subtraction arteriography. *A J R* 1982; **139**: 19–24.
12 Shafi T, Chou SY, Pososh JG, Shapiro WB. Infusion intravenous pyelography and renal functions. Effects in patients with chronic renal insufficiency. *Arch Int Med* 1978; **130**: 1218–1221.
13 Blum M, Weinberg U, Shenkman L, Hollander CS. Hyperthyroidism after iodinated contrast medium. *New Eng J Med* 1974; **291**: 24–25.
14 Coffey R, Quisling RG, Mickle JP, Hawkins IF. The cerebrovascular effects of intra-arterial CO_2 in quantities required for diagnostic imaging. *Radiology* 1984; **151**: 405–410.
15 Ramaswami G, Al-Kutobi A, Nicolaides AN *et al.* Duplex controlled angioplasty. *Eur J Vasc Surg* 1994; **8**: 457–463.

Accepted 28 December 1994